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CT-guided interventional oncology: bridging the gap between diagnosis and therapy

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The increasing imaging capabilities of cone beam and multi-detector row CT (MD-CT), such as spatial and temporal resolution and z-axis coverage, continue to evolve at a rapid pace. This enables new diagnostic applications for major diseases such as cancer, cardiovascular diseases and stroke. These evolving imaging tools can also be applied to therapeutic procedures to plan, guide, and monitor. MD-CT not only enables novel planning paradigms for procedures performed outside of the CT suite (such as bronchoscopy, colonoscopy, and external beam radiation therapy), but can also enhance procedures within the CT suite, such as percutaneous RFA. This bridges the gap between diagnosis and therapy, leading towards the goal of one-stop, image-guided medicine.

Percutaneous RFA is a leading treatment in the new minimally invasive field of image-guided “Interventional Oncology”, and the number of procedures is expected to increase exponentially [1]. Interventional radiologists (IR) are applying RFA to liver, kidney, bone, and lung tumors, often in combination with other therapies such as chemoembolization, radiation, or systemic drugs. RFA is inherently less invasive than surgery and may soon become a standard default option for certain unresectable liver tumors, which may include primary liver cancer, i.e., hepatocellular carcinoma (HCC) or metastatic spread from colorectal or other primary cancers. Unlike systemic intravenous chemotherapy, percutaneous RFA is a local treatment and can be performed with conscious sedation and local anesthesia, perhaps with less cost, morbidity, and recovery time than surgical resection.

Investigations are on-going at the NIH Clinical Center to combine MD-CT imaging capabilities with new CT-integrated devices for RFA. CT is the backbone of a prototype multimodality suite, where registration and automation tools facilitate the use of layered multimodality imaging information during interventions. The clinical goals are to:

- enable the treatment of larger tumors (> 5 cm) while decreasing the risk of under-treated tissue (especially at the tumor margins), minimizing risk to nearby structures, and reducing side effects

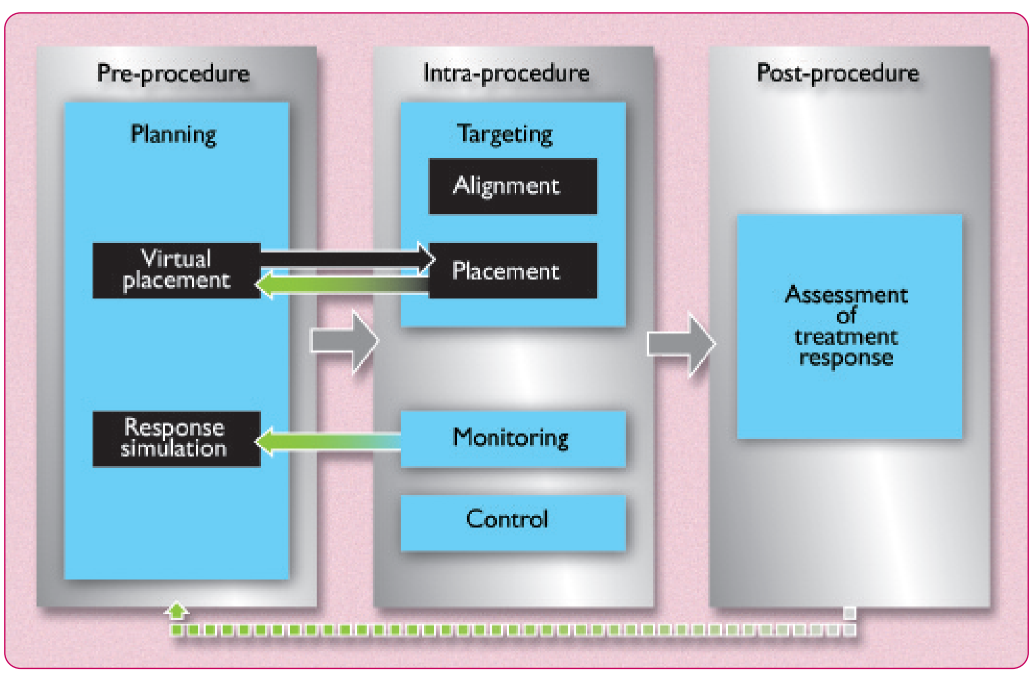
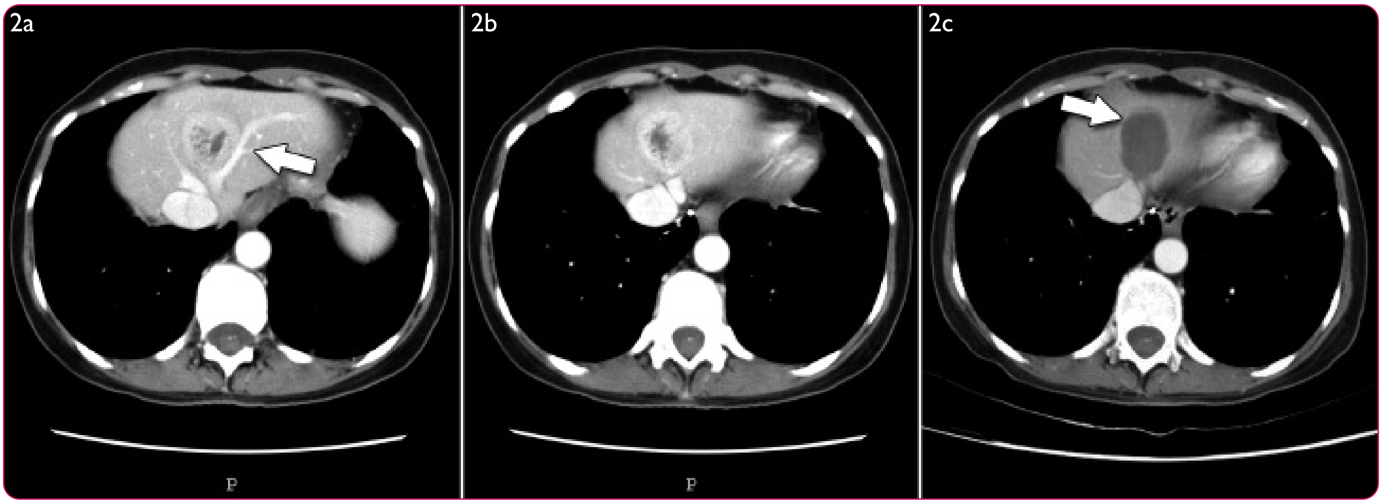


Figure 1. Pre-, intra- and post-procedure workflow for image-guided therapy. The Planning, Targeting, Monitoring, Control and Assessment stages (blue blocks) have been standardized for tumor ablation [8]. Feedback loops (green) allow the original plan to be adapted as necessary.



- increase the accuracy of electrode placement with minimal re-positioning
- increase image-based monitoring for iterative treatment adaptation
- minimize procedure time to maintain patient throughput
- facilitate translation of novel technologies to the community setting
- enable less experienced physicians to perform more complex procedures
- enhance standardization and uniform interventional oncology practice
- standardize objective treatment planning for interventional oncology
- improve patient outcome.

Methods

MD-CT can enhance the pre-, intra-, and post-procedure stages (see Figure 1) to meet these goals. The procedure stages can share technologies integrated and registered into the CT's 3D coordinate system to facilitate seamless workflow as described in the sections below.

Pre-procedure planning

Following the pre-procedure MD-CT scan (Figure 2a, b) the 3D data set is used for "on-line" planning, i.e. planning on the CT console, by interactively placing virtual RF electrodes on axial and multi-planar reformatted (MPR) views, as shown in Figure 3. Each virtual electrode comprises an electrode tip, a skin insertion point, and a spherical 50 °C isothermal treatment zone surface with an adjustable diameter.

Depending on the size and shape of the tumor, a number of virtual electrodes are placed to form a 3D ablation plan geometry based on composite overlapping spheres (Figure 4), and isothermal contours (shown in green in Figure 3) which result from the CT MPR image-sphere intersections. The isothermal contours can envelop the tumors' boundaries, while minimizing the possibility of under-treatment and the risk of applying heat to other nearby heat-sensitive structures such as bowel, nerves or the heart. The distance from the tumor margin to large blood vessels, like the middle hepatic vein shown in Figure 2a (arrow), can be measured to estimate risk of heat sink (convective heat loss from blood flow), which can lead to under-treatment of the tumor margins.

Investigations are on-going to further improve the on-line treatment planning prototype. Automated segmentation and advanced visualization of the tumor and vessels will enable automated electrode positioning. Mathematical

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Figure 2. MD-CT imaging of a primary liver tumor.

Figure 2a. Pre-procedure: contrast enhanced image showing proximity of the tumor (arrow) to the middle hepatic vein.

Figure 2b,c. Comparison of pre-procedure (b) and post-procedure (c) images to evaluate response to treatment (hypodense area).

Figure 3. On-line RFA treatment planning screen with a retrospective CT data set.

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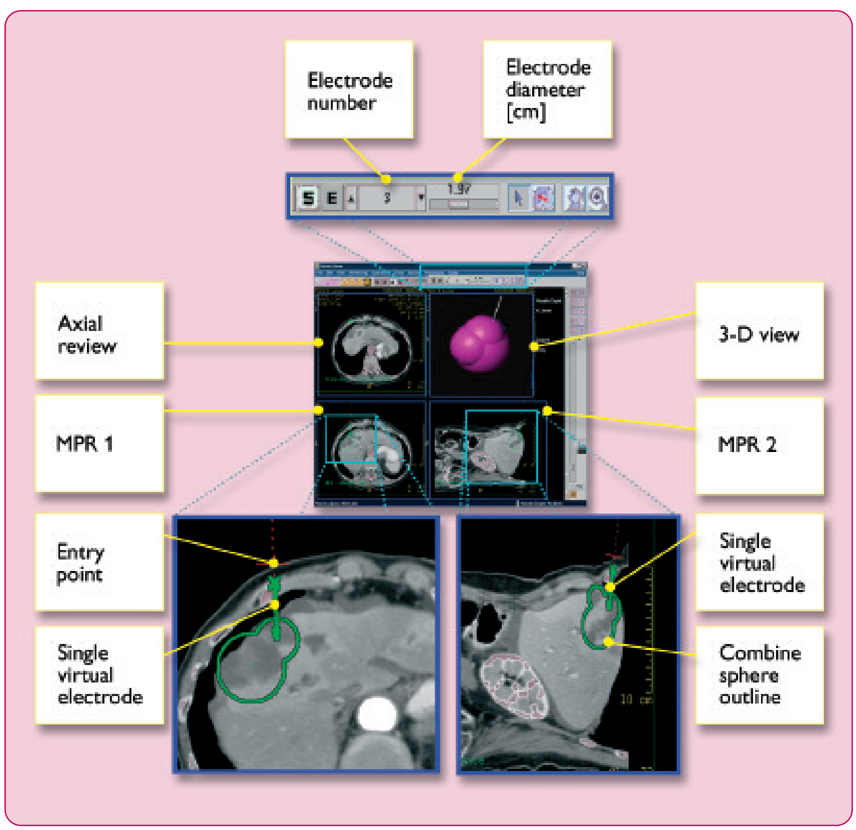

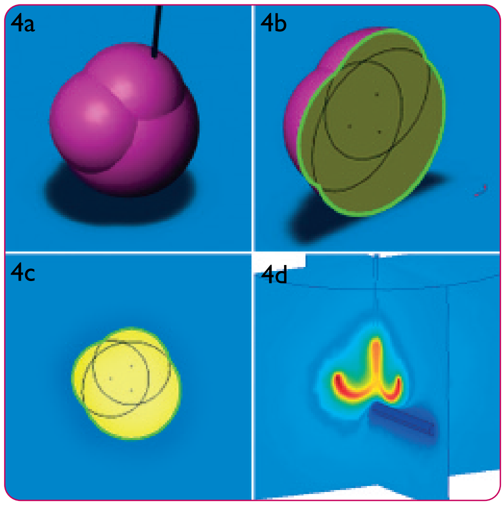

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Figure 4. Virtual electrodes are placed to form a 3D ablation plan geometry.

Figure 4a. Multiple, overlapping spherical ablations.

Figure 4b,c. Contours resulting from MPR image/sphere intersections.

Figure 4d. Finite-element model of thermal distribution for a multi-tined RFA electrode (red = high temperature) adjacent to a blood vessel (blue = relatively lower temperature). Image obtained using Comsol Multi-physics (Comsol, Inc) modeling software.

thermal models with blood flow dependencies are being used to superimpose colorized temperature maps on axial and MPR CT images. These temperature maps can predict the need for adjunctive procedures, such as fluid installation to displace organs or vascular balloon occlusion, and can be compared with direct intra-procedural temperature measurements [2]. The spherical ablation model was used for the preliminary investigation, but other shapes and sizes can be represented, such as those used for cryoablation and extracorporeal, high-intensity focused ultrasound [3].

Intra-procedure use

After planning, the interventional radiologist can use CT scanning and CT-integrated technologies for targeting, monitoring and controlling the RFA procedure.

Targeting

For targeting, 3D CT coordinates of the virtual electrodes are sent sequentially to a robot directly integrated with the CT's coordinate system (Figure 5). The robot then automatically aligns its laser with the virtual electrode's planned trajectory. The interventional radiologist then aligns the actual electrode with the laser (Figure 5b). Prior to skin puncture, the radiologist can use respiratory biofeedback displayed on the CT monitor to verify reproduction of the pre-procedure breath-hold.

Several tools are available for electrode positioning and deployment after the electrode tip punctures the skin. Volume (3D) CT fluoroscopy can improve feedback during targeting [4]. Multidetector CT enables CT fluoroscopy to be extended from 2D to 3D visualization modes at “real-time” frame rates. Figure 6 shows the simulated 3D volume rendering sequence of RFA tines being deployed in a 5-cm blood orange embedded in a CIRS Model 57 abdominal phantom (CIRS, Norfolk VA, USA).

Real-time CT imaging can be interleaved with a “mini-GPS” display; in which the 3D electrode position is graphically superimposed on registered MPR views of a previously acquired CT data set. The electrode tip is equipped with an EM sensor and is tracked in real-time with a CT-integrated field generator.

Monitoring and controlling

After the placement and deployment of an electrode, the RFA generator applies RF power to heat the target tissue. Heat accumulates when the RF current density near the electrode generates a vibrational heating effect at a faster rate than the heat can be dissipated by tissue perfusion and convection from blood flow. Typically, applying heat for 10-15 minutes can cause coagulation necrosis and destruction of tissue spanning a 4 - 5 cm diameter. Higher volumes may be achievable with novel electrodes and microwave ablation systems. The power control of RFA generators is based on temperature

Figure 5. Robot-assisted targeting: 3D CT coordinates of the virtual electrodes are sent to a robot directly integrated with the CT's coordinate system.

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Figure 5a. Six-axis robot integrated on Brilliance 16 CT scanner. The robot automatically aligns its laser with the planned trajectory.

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Figure 5b. The interventional radiologist aligns the RFA electrode with the laser.

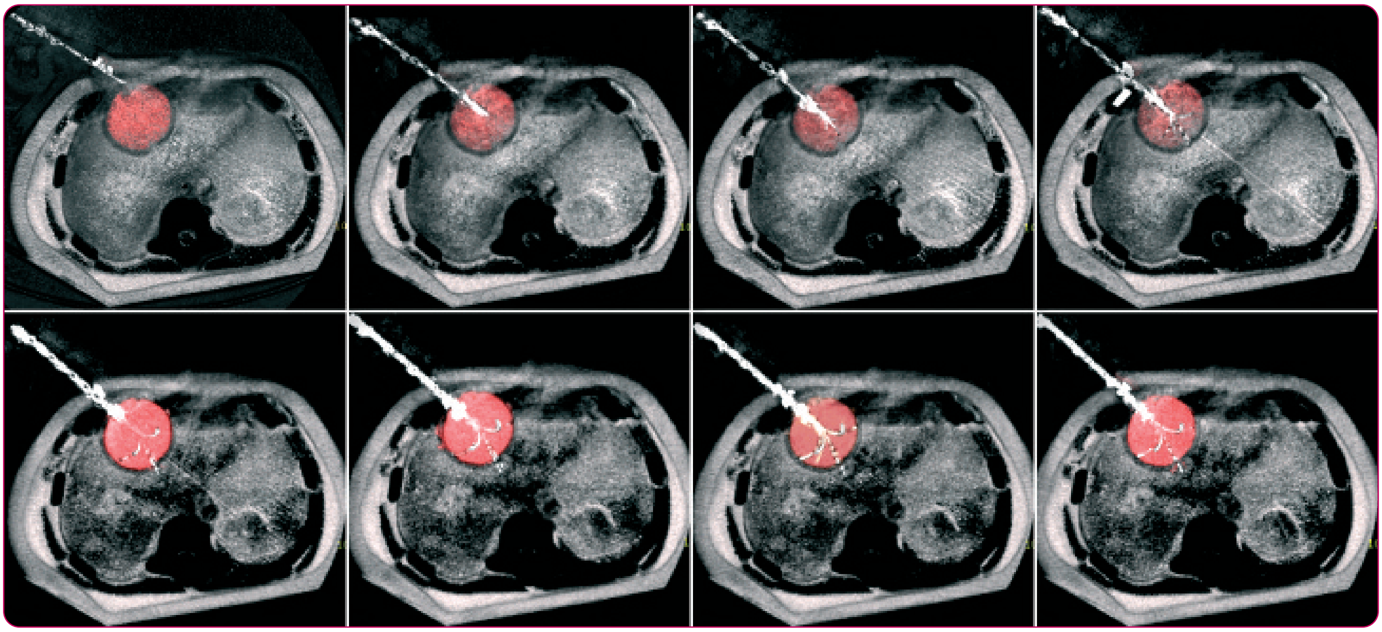

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Figure 6. Simulated volume CT fluoroscopy showing volume rendering of 3D space filling electrode tines deployed in a 5 cm blood orange embedded within a CIRS model 57 phantom.

or impedance feedback.

Real-time CT volume fluoroscopy can also be used to monitor treatment by providing dynamic visualization of contrast in the arterial, portal, or venous phase. This can be used to make real-time treatment adjustments, and the same imaging capabilities could also lead to improvements in tumor conspicuity during diagnosis with dynamic CT protocols.

Additional technologies being studied to visualize the RFA treatment effects include:
- a mini-gamma camera [6], integrated in CT coordinates, to image molecular imaging contrast agents such as nanoparticles with surface ligands that target denatured proteins or necrosis
- live 3D ultrasound registered with CT to monitor echogenic microbubble formation [7]
- exploring the use of sequential CT imaging for voxel-based temperature monitoring.

The intra-procedure phase can provide feedback to update and change the treatment plan during the treatment. Planned and actual electrode positions can be compared in the treatment planning software (See the feedback loop in Figure 1). When necessary, the positions of the virtual electrodes (Figure 3) are slightly re-adjusted to match the actual electrode positions shown in the image. Adjusting each virtual electrode updates the combined treatment contours so that the interventionalist can verify that the planned tumor coverage is sufficient.

Post procedure

After treatment, for the acute and long-term follow up, a contrast-enhanced CT scan can verify that the tumor has received sufficient treatment (Figure 2c). Estimations of tumor size can be longitudinally tracked with sequential CT scans and established tumor size measuring criteria (e.g., RECIST or WHO), or other 3D criteria [8].

Recently, PET-CT or SPECT-CT imagers have been used on some protocols to track tumor size and viability with potentially more accuracy than CT alone [9]. These hybrid image devices can help further differentiate a heterogeneous tumor, and indicate the potential need for re-treatment based on functional, metabolic or molecular information.

Conclusion

Advances in CT imaging, together with seamlessly CT-integrated technologies such as pre-planning software and navigation tools, will enable tumor treatment to be less invasive, faster, more targeted, and truly image-guided.

Technological advances should be judged by their ability to cost-effectively improve patient outcomes, physicians' abilities and efficient throughput.

The prototype CT-integrated system provides an image-guided framework for investigation of new concepts for RFA and other minimally or non-invasive procedures. This framework could eventually be extended to other multi-modality image-guided ablative therapies and could have spin-off applications for diagnosis.

The interventional radiology suite of the future, based on a CT “backbone”, will allow for efficient use of multimodality information in a streamlined setting that should be readily adaptable to current standard approaches, practices and paradigms. This CT-based multimodality interventional suite will provide a cost-effective alternative to other more complex, expensive, cumbersome, and technologically immature approaches.

As advances in CT are integrated with other imaging devices and tools, tumor diagnosis and treatment could be intimately intertwined with one-stop, point-and-click, semi-automated, image-guided therapy.

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